REMARKS/ARGUMENTS

Claim 63 is canceled without prejudice. Claims 29-31, 35-38, 42, 57, 59, 64, and 68 are amended. Claims 29-42, 55-62, 64-66, and 68-70 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Claims 29-34, 36-38, 41-42, and 55-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,622,826 (Varma). This rejection is moot with respect to claim 63 due to the cancellation of the claim. With respect to claims 29-34, 36-38, 41-42, and 55-56, this rejection is respectfully traversed.

Independent claim 29 has been amended to clarify the term "modified substrate." Amended claim 29 requires a step of modifying the surface of the substrate by introducing a functionality selected from a group consisting of an amino group, a carboxyl group, a thiol group, and their derivatives on the surface to obtain a modified surface.

This amendment is fully supported by the specification. On page 7, lines 6-10, the specification states:

> The direct adsorption is further improved by modifying the substrates prior to contacting them with biopolymers. The **substrates may be modified by introducing a functionality selected from a group consisting of: amino, carboxyl, thiol, and their derivatives**. In one embodiment, the substrate is modified by introduction of an amine group.

Also, the specification describes specific methods, such as plasma discharge, that may be used to modify the substrates (page 7, lines 11-22).

Varma does not anticipate claim 29, because he does not teach a modified surface, which is obtained by introducing a functionality selected from a group consisting of an amino group, a carboxyl group, a thiol group, and their derivatives. Instead, Varma teaches the modification of a surface of a platinum, glass, or aminated polyprolylene with isocyanate or isothiocyanate (Abstract and column 2, line 51 - column 3, line 35).

Additionally, Varma does not anticipate claim 29, because he does not teach the immobilization of a biopolymer on the modified surface by adsorption as required by step (c) of claim 29. Instead, Varma teaches covalent binding of nucleic acids with reactive isocyanate or isothiocyanate moieties of the modified substrate (column 2, lines 55-56; column 6, lines 61-62).

Varma doesn't make the present invention obvious. It is an unexpected discovery of the present invention that substrates with the modified surfaces, such as plasma-aminated polypropylene and polysterene substrates, are capable of direct and stable adsorption of biopolymers without the need for chemical linkers and additional fixing steps, such as those commonly used in enzyme-linked immunosorbent assays (ELISA) (page 8, lines 13-21). Consequently, the present invention provides a number of advantages over the conventional methods. The advantages include, for example, a simplification of the production of polypeptide arrays and a decrease in their manufacturing costs (page 5, lines 25-30).

Varma teaches a two-step immobilization of nucleic acids on aminated polypropylene substrates. The first step includes the further modification of aminated polypropylene by reaction with isocyanate or an isothiocyanate to obtain an activated surface. The second step is a covalent binding of a nucleic acid derivatized to contain an amino group with the reactive groups on the activated surface (column 3, lines 23-34; column 18, lines 7-25). These teachings of Varma demonstrate that, prior to the present invention, those skilled in the art did not expect that biopolymers could be immobilized directly on aminated polypropylene substrates by adsorption and without the need for reactive groups such as isocyanates or isothiocyanates.

Thus, based on the teachings of Varma and without the hindsight of the present invention, those skilled in the art would not have realized that substrates with a modified surface having a functionality selected from a group consisting of an amino group, a carboxyl group, a thiol group, and their derivatives, can be used without further derivatization for the immobilization of biopolymers. Therefore,

Varma does not anticipate or make present claim 29 obvious. Claims 30-34, 36-38, 41-42, and 55-56 depend from claim 29, directly or indirectly, and are patentable over Varma for at least the same reasons as claim 29.

Claims 64-68 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,970,144 (Fareed). This rejection is respectfully traversed.

The Examiner appears to believe that because Fareed teaches air-drying of a protein solution on the bottom of wells in microtiter dishes, it anticipates claim 64. The Examiner disregarded the term "modified substrate" in claim 64, because the Examiner found it to be unclear. The Examiner noted, "[a]lthough the claims are interpreted in light of the specification, limitations from the specification are not read into the claims." Although applicant disagrees that the term "modified substrate" is unclear for the reasons of record, in order to expedite the prosecution of the present invention, applicant amended claim 64. Amended claim 64 requires a step of modifying the surface of the substrate by introducing a functionality selected from a group consisting of an amino group, a carboxyl group, a thiol group, and their derivatives on the surface to obtain a modified surface.

Additionally, the Examiner requested evidence supporting applicant's statement that it was unexpected in the art, prior to the present invention, that modified substrates, such as plasma-aminated polypropylene and polysterene substrates, are capable of direct and stable adsorption of polypeptides without the need for additional fix steps. Applicant believes that such evidence is presented in Varma references.

As discussed above, Varma teaches that further chemical derivatization of aminated polypropylene substrates by reaction with isocyanate or an isothiocyanate is required for stable immobilization of nucleic acids on the substrate. These teachings of Varma demonstrate that, prior to the present invention, those skilled in the art did not expect that biopolymers could be immobilized directly on aminated polypropylene substrates by adsorption and without the need for reactive groups such as isocyanates or isothiocyanates.

Fareed does not anticipate independent claim 64, because he does not teach a modified surface, which is obtained by introducing a functionality selected from a group consisting of an amino group, a carboxyl group, a thiol group, and their derivatives. Additionally, Fareed does not anticipate instant claim 64 because it does not teach "contacting either the probe or target polypeptide with the modified surface of the substrate and drying the substrate whereby either the probe or target polypeptide directly adsorbs and immobilizes on the modified surface without additional fixing steps."

Instead, Fareed teaches using conventional microtiter dishes for "typical ELISA assay" (column 11, lines 34-43). Such conventional microtiter plates do not have modified surfaces as defined in the present invention. Furthermore, in a "typical ELISA assay," a protein is not immobilized by drying as in the present invention, but rather chemically fixed onto the dish (see step 3 of the ELISA procedure in columns 13-14 of Fareed).

Fareed does not suggest instant claim 64, because he does not suggest the immobilization of polypeptides by drying. At most, Fareed teaches a conventional ELISA assay with a two-step immobilization of protein. The first step involves an overnight drying of 50 µl of the protein solution in the wells of a conventional microplate and the second step involves the immobilization of protein by "filling the wells with absolute methanol to fix the protein onto the dish" (column 14, lines 1-2). Based on such teaching, those skilled in the art would have not been motivated to modify the material of standard microplates to arrive at substrates with the modified surfaces of the present invention, much less to omit the protein-fixing step of the standard ELISA protocol without the hindsight of the present invention.

Therefore, Fareed does not teach or suggest the immobilization of polypeptides by drying on modified substrates and, thus, does not anticipate or make present claim 64 obvious. Claims 65-66 and 68 depend from claim 64, directly or indirectly, and are patentable over Fareed for at least the same reasons as claim 64.

Claims 39-40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Varma in view of U.S. Patent No. 6,197,501 (Cremer). This rejection is respectfully traversed.

As discussed above, claim 29 is patentable over Varma. Cremer does not remedy the defects of Varma and is not relied upon by the Examiner for such. The Examiner cites Cremer for the teaching of fluorescence labeling and using a CCD camera. Cremer does not teach or suggest adsorption of a biopolymer on a modified surface, which is obtained by introducing a functionality selected from a group consisting of an amino group, a carboxyl group, a thiol group, and their derivatives. Therefore, claim 29 is patentable over Varma in view of Cremer. Claims 39-40 depend from claim 29 and are patentable over the cited references for at least the same reasons as claim 29.

Claim 35 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Varma in view of U.S. Patent No. 6,013,789 (Rampal). This rejection is respectfully traversed.

As discussed above, claim 29 is patentable over Varma. Rampal does not remedy the defects of Varma and is not relied upon by the Examiner for such. The Examiner cites Rampal for the teaching of ELF. Therefore, claim 29 is patentable over Varma in view of Rampal. Claim 35 depends from claim 29 and is patentable over the cited references for at least the same reasons as claim 29.

Claims 57-62 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Varma and claims 68-70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fareed. This rejection is respectfully traversed.

As discussed above, independent claim 29 is patentable over Varma and independent claim 64 is patentable over Fareed. Claims 57-62 depend from claim 29 and are patentable over Varma for at least the same reasons as claim 29. Claims 68-70 depend from claim 64 and are patentable over Fareed for at least the same reasons as claim 64.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
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